

(FILE 'HOME' ENTERED AT 18:17:38 ON 07 JUL 2003)

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 18:18:22 ON 07 JUL 2003

E JACKOWSKI/AU

E JACKOWSKI G/AU

L1 155 S E3

L2 0 S D E3

FILE 'GENBANK' ENTERED AT 18:44:10 ON 07 JUL 2003

SET NOTICE DISPLAY 1

SET NOTICE LOGIN DISPLAY

FILE 'GENBANK' ENTERED AT 19:01:37 ON 07 JUL 2003

SET NOTICE DISPLAY 1

SET NOTICE LOGIN DISPLAY

E MARSHALL/AU

E MARSHALL J/AU

E MARSHALL J/AU

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 19:06:41 ON 07 JUL 2003

E MARSHALL J/AU

FILE 'GENBANK' ENTERED AT 19:09:50 ON 07 JUL 2003

L3 0 S MARSHALL J/AU

E MARSHALL J/AU

L4 19 S E2

E MARSHALL J/AU

L5 19 S E2

=>

# Registry Record for seq1

DAVIS 09/933,366

=> d sqide l18

L18 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS

RN 535944-44-6 REGISTRY

CN L-Leucine, L-lysyl-L-leucyl-L-valyl-L-prolyl-L-phenylalanyl-L-alanyl-L-threonyl-L-.alpha.-glutamyl-L-leucyl-L-histidyl-L-.alpha.-glutamyl-L-arginyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 1: PN: W003046000 SEQID: 1 claimed protein

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 13

PATENT ANNOTATIONS (PNTE):

Sequence |Patent

Source |Reference

Not Given|W02003046000

|claimed

|SEQID 1

SEQ 1 KLVPFATELH ERL

HITS AT: 1-13

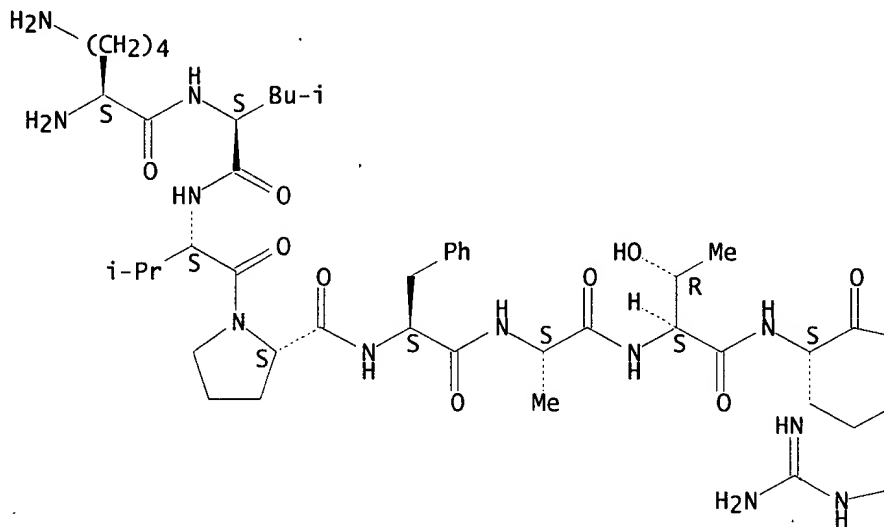
MF C72 H117 N19 O19

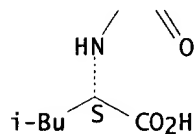
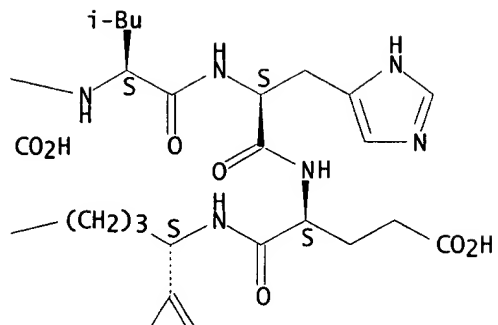
SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A





\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1957 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

=> d que 117

L13	53	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	KLVPFATELHERL/SQSP	
L14	15	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L13	
L15	1	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L14 AND INSULIN(2A)RESIST?	← 1 cite
L16	2	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L14 AND INSULIN	
L17	15	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	(L14 OR L15 OR L16)	15 cites total

=&gt; d ibib abs hitstr 1

L17 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2003:448587 HCAPLUS  
Correction of: 2003:177120

ACCESSION NUMBER: 138:200022

TITLE: Differentially expressed nucleic acids and their  
encoded proteins associated with pain and their use in  
screening for regulatory agentsINVENTOR(S): Woolf, Clifford; D'Urso, Donatella; Befort, Katia;  
Costigan, Michael

PATENT ASSIGNEE(S): The General Hospital Corporation, USA; Bayer AG

SOURCE: PCT Int. Appl., 1017 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003016475	A2	20030227	WO 2002-XA25765	20020814
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
WO 2003016475	A2	20030227	WO 2002-US25765	20020814
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.:

US 2001-312147P	P	20010814
US 2001-346382P	P	20011101
US 2001-333347P	P	20011126
WO 2002-US25765	A	20020814

AB The present invention relates to human and rat nucleic acid sequences which are related to pain and which are differentially expressed during pain. The nucleic acids are differentially expressed by at least  $\pm 1.4$ -fold in any or all of the following conditions using the Affymetrix human U95, murine U74 and rat U34 GeneChip arrays: axotomy, spared nerve injury, chronic constriction, spinal segmental nerve lesion, and inflammatory pain models. The invention further relates to methods of identifying nucleic acid sequences which are differentially expressed during pain, microarrays comprising such differentially expressed sequences, and methods of screening agents for the ability to regulate the expression of such differentially expressed sequences. [This abstr.]

record is one of seven records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.].

IT 538434-40-1

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(amino acid sequence; differentially expressed nucleic acids and their encoded proteins assocd. with pain and their use in screening for regulatory agents)

RN 538434-40-1 HCAPLUS

CN INDEX NAME NOT YET ASSIGNED

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

=> d ibib abs hitrn 2-15

L17 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2003:434604 HCAPLUS

DOCUMENT NUMBER: 139:3224

TITLE: Apolipoprotein biopolymer markers predictive of insulin resistance

INVENTOR(S): Jackowski, George; Marshall, John

PATENT ASSIGNEE(S): Syn.X Pharma, Inc., Can.

SOURCE: PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003046000	A2	20030605	WO 2002-CA1660	20021031
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2001-993366 A 20011121

AB The instant invention involves the use of a combination of preparatory steps in conjunction with mass spectroscopy and time-of-flight detection procedures to maximize the diversity of biopolymers which are verifiable within a particular sample. The cohort of biopolymers verified within such a sample is then viewed with ref. to their ability to evidence at least one particular disease state; thereby enabling a diagnostician to gain the ability to characterize either the presence or absence of said at least one disease state relative to recognition of the presence and/or the absence of said biopolymer, predict disease risk assessment, and develop therapeutic avenues against said disease.

IT 535944-44-6

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(apolipoprotein biopolymer markers predictive of **insulin resistance**)

L17 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 2002:716295 HCAPLUS  
 DOCUMENT NUMBER: 137:246068  
 TITLE: Genes associated with cardiovascular disease and polymorphisms in them and their predictive and therapeutic uses  
 INVENTOR(S): Braun, Andreas; Bansal, Aruna; Kleyn, Patrick W.  
 PATENT ASSIGNEE(S): Sequenom, Inc., USA  
 SOURCE: PCT Int. Appl., 199 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002072604	A2	20020919	WO 2002-US6728	20020305

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003036057	A1	20030220	US 2001-802640	20010309
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PRIORITY APPLN. INFO.: US 2001-802640 A 20010309

AB Genes and polymorphisms assocd. with cardiovascular disease, methods that use the polymorphism to detect a predisposition to developing high cholesterol, low HDL or cardiovascular disease, to profile the response of subjects to therapeutic drugs and to develop therapeutic drugs are provided.

IT 459469-93-3

RL: PRP (Properties)

(unclaimed protein sequence; genes assocd. with cardiovascular disease and polymorphisms in them and their predictive and therapeutic uses)

L17 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:429472 HCAPLUS  
 DOCUMENT NUMBER: 137:29063  
 TITLE: Cloning and cDNA and deduced amino acid sequences of 32 human secreted proteins  
 INVENTOR(S): Ni, Jian; Baker, Kevin P.; Birse, Charles E.; Ebner, Reinhard; Fiscella, Michele; Komatsoulis, George A.; Lafleur, David W.; Moore, Paul A.; Olsen, Henrik S.; Rosen, Craig A.; Ruben, Steven M.; Soppet, Daniel R.; Young, Paul E.; Wei, Ping; Florence, Kimberly A.  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 458 pp., Cont.-in-part of Appl. No. PCT/US00/36013.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002068319	A1	20020606	US 2001-800729	20010308
WO 2001021658	A1	20010329	WO 2000-US26013	20000922

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-155709P P 19990924  
WO 2000-US26013 A2 20000922

AB The present invention relates to 32 novel human secreted proteins and isolated nucleic acids contg. the coding regions of the genes encoding such proteins. Tissue distribution, sequence homologies, and preferred epitope sites are provided for the secreted proteins, as well as chromosomal mapping of some of the genes. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins in bacterial, insect, and mammalian cells. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to these novel human secreted proteins. High-throughput screening assays are also provided for various putative activities of the secreted proteins.

IT 429969-67-5 429969-68-6

RL: PRP (Properties)

(unclaimed protein sequence; cloning and cDNA and deduced amino acid sequences of 32 human secreted proteins)

L17 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:763012 HCAPLUS

DOCUMENT NUMBER: 135:314444

TITLE: Polymorphisms in the human apolipoprotein A-IV (APOA4) gene as drug targets

INVENTOR(S): Bentivegna, Steven C.; Choi, Julie Y.; Kliem, Stefanie E.; Koshy, Beena

PATENT ASSIGNEE(S): Genaisance Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 71 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001077124	A2	20011018	WO 2001-US10670	20010403
WO 2001077124	A3	20021003		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,



BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 AU 2001051245 A5 20011023 AU 2001-51245 20010403  
 PRIORITY APPLN. INFO.: US 2000-194362P P 20000405  
 WO 2001-US10670 W 20010403

AB Ten novel single nucleotide polymorphisms in the human apolipoprotein A-IV (APOA4) gene were discovered by characterizing the APOA4 gene found in genomic DNAs isolated from Index Repository that contains immortalized cell lines from one chimpanzee and 93 human individuals. Comps. and methods for detecting one or more of these polymorphisms are also disclosed. Allele-specific oligonucleotides for hybridization, amplification, or primer-extension are provided for genotyping or haplotyping the APOA4 gene. In addn., various genotypes and haplotypes for APOA4 gene that exist in the population are described.

IT 110909-99-4

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (amino acid sequence; polymorphisms in human apolipoprotein A-IV (APOA4) gene as drug targets)

L17 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:228926 HCAPLUS

DOCUMENT NUMBER: 134:232738

TITLE: Cloning and cDNA and deduced amino acid sequences of 32 human secreted proteins

INVENTOR(S): Ni, Jian; Baker, Kevin P.; Birse, Charles E.; Ebner, Reinhard; Fiscella, Michele; Komatsoulis, George A.; Lafleur, David W.; Moore, Paul A.; Olsen, Henrik S.; Rosen, Craig A.; Ruben, Steven A.; Soppet, Daniel R.; Young, Paul E.; Wei, Ping; Florence, Kimberly A.

PATENT ASSIGNEE(S): Human Genome Sciences, Inc., USA

SOURCE: PCT Int. Appl., 878 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001021658	A1	20010329	WO 2000-US26013	20000922
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1218408	A1	20020703	EP 2000-965302	20000922
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
JP 2003511012	T2	20030325	JP 2001-525231	20000922
US 2002068319	A1	20020606	US 2001-800729	20010308
PRIORITY APPLN. INFO.:			US 1999-155709P P 19990924	
			WO 2000-US26013 W 20000922	

AB The present invention relates to 32 novel human secreted proteins and isolated nucleic acids contg. the coding regions of the genes encoding such proteins. Tissue distribution, sequence homologies, and preferred epitope sites are provided for the secreted proteins, as well as chromosomal mapping of some of the genes. Also provided are vectors, host

cells, antibodies, and recombinant methods for producing human secreted proteins in bacterial, insect, and mammalian cells. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to these novel human secreted proteins. High-throughput screening assays are also provided for various putative activities of the secreted proteins.

IT 102305-81-7 330232-11-6

RL: PRP (Properties)

(unclaimed protein sequence; cloning and cDNA and deduced amino acid sequences of 32 human secreted proteins)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:12599 HCAPLUS

DOCUMENT NUMBER: 134:96929

TITLE: human Apolipoprotein a-iv-related protein: polypeptide, polynucleotide sequences and biallelic markers with applications for genotyping

INVENTOR(S): Yen, Frances; Denison, Blake; Bour, Barbara; Bihain, Bernard; Bougueleret, Lydie; Duclert, Aymeric; Dumas Milne Edwards, Jean-Baptiste

PATENT ASSIGNEE(S): Genset, Fr.

SOURCE: PCT Int. Appl., 261 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000803	A2	20010104	WO 2000-IB1011	20000621
WO 2001000803	A3	20011227		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

WO 2000037491	A2	20000629	WO 1999-IB2058	19991220
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WO 2000037491	A3	20010920		
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6455280	B1	20020924	US 2000-750580	20001228
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PRIORITY APPLN. INFO.:

US 1999-141032P	P	19990625
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WO 1999-IB2058	W	19991220
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US 1999-469099	A	19991221
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US 1998-113686P	P	19981222
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US 2000-599362	A2	20000621
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WO 2000-IB1011 A2 20000621

AB The invention provides the genomic sequence of AA4RP, AA4RP cDNAs and AA4RP polypeptides. This protein is a homolog of the regeneration associated protein 3 (RAP3) which is a secreted protein whose plasma level increases after liver damage. In addn. homologous recombination is used to target and disrupt the AA4RP gene. Further the invention provides polynucleotides including biallelic markers derived from the AA4RP gene and from genomic regions flanking the gene. This invention also provides polynucleotides and methods suitable for genotyping a nucleic acid contg. sample for one or more biallelic markers of the invention. Further, the invention provides methods to detect a statistical correlation between a biallelic marker allele and a phenotype and/or between a biallelic marker haplotype and a phenotype. The invention also relates to diagnostic methods for detg. whether an individual is at risk of developing a lipid metab. related disorder and/or a liver related disorder, or whether said individual suffers from a lipid metab. related disorder and/or a liver related disorder as a result of a polymorphism in the AA4RP gene. Monoclonal antibodies were generated by hybridoma fusion and polyclonal antibodies were generated by immunization. Genotyping is accomplished by using a hybridization assay, a sequencing assay, a microsequencing assay, and an enzyme-based mismatch detection assay. Haplotypes are detd. by asym. PCR amplification, double PCR amplification of specific alleles, the Clark algorithm, or an expectation-maximization algorithm. Tests on effect of AA4Rp on LSR(lipolysis stimulated receptor) are performed. The effects of AA4RP on mice fed a high-fat diet were performed. In addn., the effects of AA4RP on plasma free fatty acids are described. The effects of AA4RP on plasma leptin and insulin levels were also studied.

IT 318299-83-1 318299-84-2

RL: PRP (Properties)

(unclaimed sequence; human Apolipoprotein a-iv-related protein, polypeptide, polynucleotide sequences and biallelic markers with applications for genotyping)

L17 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1993:643750 HCAPLUS

DOCUMENT NUMBER: 119:243750

TITLE: Baboon apolipoprotein A-IV. Identification of Lys76 .fwdarw. Glu that distinguishes two common isoforms and detection of length polymorphisms at the carboxyl terminus

AUTHOR(S): Hixson, James E.; Kammerer, Candace M.; Mott, Glen E.; Britten, Marjorie L.; Birnbaum, Shifra; Powers, Patricia K.; VandeBerg, John L.

CORPORATE SOURCE: Dep. Genet., Southwest Found. Biomed. Res., San Antonio, TX, 78228-0147, USA

SOURCE: Journal of Biological Chemistry (1993), 268(21), 15667-73

CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Various protein isoforms have been identified for human apolipoprotein A-IV (apoA-IV). However, investigations of their physiol. effects have been limited because of low frequencies for many of the apoA-IV variants. Recent discovery of extensive variation in baboon apoA-IV using isoelec. focusing (IEF) makes this primate species an excellent model for genetic studies of apo-A-IV. In this study, the mol. basis for net charge differences between two common apoA-IV isoforms (I and E) was detd. by cloning and sequencing of intestinal cDNAs from homozygous baboons. As A .fwdarw. G substitution was found in the third amphipathic repeat of the E

isoform. This substitution causes a Lys .fwdarw. Glu substitution at amino acid position 76 (Lys76 .fwdarw. Glu), adding two neg. charges to the E isoform compared to the I isoform, consistent with their relative mobilities on IEF gels. Restriction isotyping was used to identify the substitution in leukocyte DNA from 15 baboons that had been typed by IEF, thus verifying Lys76 .fwdarw. Glu as the basis for the charge differences between the I and E isoforms. Physiol. effects of the Lys76 .fwdarw. Glu substitution on high d. lipoprotein-C levels were investigated in 431 baboons carrying the E and I isoforms. These studies revealed that the I isoform was assocd. with higher levels of high d. lipoprotein-C on a high cholesterol, satd. fat diet(p = 0.04). The cDNA sequences showed that the carboxyl terminus of baboon apoA-IV contains a region of hydrophilic repeats (Glu-Gln-X-gln) that is the largest yet found in any species (nine repeats compared to three to five repeats in human, mouse, and rat). A common length polymorphism was identified that inserts a single amino acid to form a five amino acid repeat. This is the first report of this type of length variation (insertion of a single amino acid rather than insertion of an entire repeat) in this region. In addn., a rare variant was found that inserts an entire four-amino-acid repeat, similar to the human apoA-IV-0 isoform.

IT 151086-88-3 151086-89-4

RL: PRP (Properties)

(amino acid sequence of, high-d. lipoprotein C serum level in relation to)

L17 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1993:620056 HCAPLUS

DOCUMENT NUMBER: 119:220056

TITLE: Polypeptides derived from human A-IV apolipoprotein, preparation with recombinant cells, and use as antithrombotics and anticholesteremics

INVENTOR(S): Deneffe, Patrice; Guinet, Francoise; Latta, Martine; Murry-Brelier, Anne

PATENT ASSIGNEE(S): Rhone-Poulenc Rorer S.A., Fr.

SOURCE: PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9315198	A1	19930805	WO 1993-FR73	19930126
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2686605	A1	19930730	FR 1992-806	19920127
FR 2686605	B1	19940311		
EP 624194	A1	19941117	EP 1993-904117	19930126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 07503367	T2	19950413	JP 1993-512981	19930126
PRIORITY APPLN. INFO.:			FR 1992-806	19920127
			WO 1993-FR73	19930126

AB Derivs. of human apolipoprotein A-IV comprising that protein encoded by all exons except the 1st two modified by substitution, terminal deletion, deletion of 1 or 2 helixes, and/or fusion to an heterologous protein are described. These proteins may be prepd. with recombinant cells and used to treat hypercholesterolemia or as antithrombotics. Many human apolipoprotein A-IV derivs. were prepd. with recombinant E. coli and tested for HDL receptor binding and for alteration of cholesterol efflux

from murine adipocytes.

- IT 150826-93-0P 150826-94-1P, 13-376-Lipoprotein A-IV  
(human clone .lambda.AIV-2) 150826-95-2P 150826-96-3P  
150826-97-4P 150826-98-5P 150826-99-6P  
150827-03-5P 150827-04-6P 150827-05-7P  
150827-06-8P 150827-07-9P 150827-08-0P  
150827-09-1P 150827-10-4P 150827-11-5P  
150827-12-6P 150827-13-7P 150827-14-8P  
150827-15-9P 150827-16-0P 150827-17-1P  
150827-18-2P 150827-19-3P 150827-20-6P  
RL: BAC (Biological activity or effector, except adverse); BMF  
(Bioindustrial manufacture); BSU (Biological study, unclassified); THU  
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
(Uses)  
(manuf. with recombinant cells of, use as antithrombotics and  
anticholesteremics of)
- IT 150826-91-8D, analogs and fusion products  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); BIOL (Biological study)  
(manuf. with recombinant cells of, use as antithrombotics and  
anticholesteremics of)

L17 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1993:421874 HCAPLUS  
DOCUMENT NUMBER: 119:21874  
TITLE: Nucleotide sequences of the *Macaca fascicularis*  
apolipoprotein C-III and A-IV genes  
AUTHOR(S): Osada, Jesus; Pocovi, Miguel; Nicolosi, Robert J.;  
Schaefer, Ernst J.; Ordozas, Jose Maria  
CORPORATE SOURCE: Lipid Metab. Lab., U.S.D.A., Hum. Nutr. Cent. on Aging  
at Tufts Univ., Boston, MA, USA  
SOURCE: Biochimica et Biophysica Acta (1993), 1172(3), 335-9  
CODEN: BBACAQ; ISSN: 0006-3002  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The cynomolgus monkey (*Macaca fascicularis*) apolipoprotein C-III and  
apolipoprotein A-IV genes have been isolated from a cynomolgus genomic DNA  
library and completely sequenced. These genes span 3.1 and 2.8 kilobases  
(kb), resp. Apolipoprotein C-III gene is interrupted by three intervening  
sequences of 613, 135 and 1699 bp, resp. The open reading frame encodes a  
protein of 99 amino acids which is 87% similar to the human. The  
cynomolgus mature protein is 79 residues long. Thr-74 is also present and  
might allow the formation of the O-glycosidic linkage obsd. in the human  
protein. The apolipoprotein A-IV gene consists of two intervening  
sequences of 352 and 774 bp, resp. The open reading frame encodes a  
protein of 429 amino acids which is 87% similar to the human. The  
cynomolgus mature protein is 409 residues long, 33 amino acids longer than  
the human, due to an insertion of 33 residues in its COOH-terminal region.  
This insertion is mainly composed of glutamine and glutamic acid, which  
confers cynomolgus apolipoprotein a higher hydrophilicity.

- IT 148242-00-6, Preapolipoprotein A-IV (*Macaca fascicularis* clone  
EMBL3A-IV5)  
RL: PRP (Properties)  
(amino acid sequence of)

L17 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1989:627408 HCAPLUS  
DOCUMENT NUMBER: 111:227408  
TITLE: The primary structure of human apolipoprotein A-IV  
AUTHOR(S): Yang, Chao Yuh; Gu, Zi Wei; Chong, Ilson; Xiong,

CORPORATE SOURCE: Weijun; Rosseneu, Maryvonne; Yang, Hui Xin; Lee, Bo  
 Rong; Gotto, Antonio M., Jr.; Chan, Lawrence  
 SOURCE: Dep. Med., Baylor Coll. Med., Houston, TX, 77030, USA  
 Biochimica et Biophysica Acta (1989), 1002(2), 231-7  
 CODEN: BBACAQ; ISSN: 0006-3002

DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Human apolipoprotein (apo) A-IV was purified from chylous ascites fluid. Proteolytic peptides produced by trypsin and Staphylococcus aureus V8 proteinase digestions were purified by HPLC and sequenced. Human apoA-IV contains 376 amino acid residues. The peptide-derived sequence generally matches 2 previously reported DNA-derived amino acid sequences except for discrepancies in 5 positions. In order to examine these discrepancies further, 1 complete apoA-IV cDNA clone and another partial clone were sequenced. The peptide-derived sequence is accurate. Sequencing errors probably account for some of the discrepancies between the 2 primary sequences predicted by earlier nucleotide analyses. In certain positions, however, sequence heterogeneity or cloning artifact cannot be excluded.

IT 123781-21-5, Lipoprotein A-IV (human clone .lambda.AIV-1 protein moiety) 123781-22-6, Lipoprotein A-IV (human clone .lambda.AIV-2 protein moiety) 123781-23-7  
 RL: PRP (Properties)  
 (amino acid sequence of)

L17 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1987:592041 HCAPLUS

DOCUMENT NUMBER: 107:192041

TITLE: Structure and expression of the human apolipoprotein A-IV gene

AUTHOR(S): Elshourbagy, Nabil A.; Walker, David W.; Paik, Young Ki; Boguski, Mark S.; Freeman, Mark; Gordon, Jeffrey I.; Taylor, John M.

CORPORATE SOURCE: Univ. California, San Francisco, CA, 94140-0608, USA  
 SOURCE: Journal of Biological Chemistry (1987), .262(17), 7973-81

CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The human apolipoprotein (apo) A-IV gene was isolated from a cosmid library and its complete nucleotide sequence was detd. The gene contains 3 exons of 162, 127, and 1180 nucleotides sepd. by 2 introns of 357 and 777 nucleotides. A sequence polymorphism was identified in the 3'-noncoding portion of the third exon. The human apoA-IV gene lacks an intron in the area encoding the 5' nontranslated region of its mRNA, which distinguishes it from all the other human apolipoprotein genes whose sequences are known. Comparison matrix anal. of the human apo-A-IV gene sequence revealed evidence for an ancestral 11-nucleotide repeat unit that spans the third exon. These repeated sequences are much more highly conserved than those present in either rat apoA-IV or in any other human apolipoprotein genes. Optimal alignments of the 5'-flanking regions of the rat and human apoA-IV genes disclosed multiple deletions in the rat sequence as well as a highly conserved region of 90 nucleotides (90% sequence identity) located within 170 nucleotides of the start site of transcription. The 5'-flanking regions of the human and rat apoA-IV genes were ligated to the bacterial chloramphenicol acetyltransferase gene, then transfected into different cultured cells. The apoA-IV gene sequences elicited preferential expression of chloramphenicol acetyltransferase activity when introduced into intestinally derived Caco-2 cells and liver-derived Hep-G2 cells, consistent with the tissue specificity of the native gene. Anal. of deletion mutants of the human apoA-IV 5' flanking

region indicated that regions from -293 to -233 and from -127 to -60 upstream of the transcription start site contain sequences required for max. gene expression. These findings on the structure and expression of rat and human apoA-IV should prove useful in studying the control of the apoA-IV gene.

IT 101551-39-7, Lipoprotein A-IV (human protein moiety)

110909-99-4

RL: PRP (Properties)

(amino acid sequence of)

L17 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1987:62019 HCAPLUS

DOCUMENT NUMBER: 106:62019

TITLE: Structure, evolution, and polymorphisms of the human apolipoprotein A4 gene (APOA4)

AUTHOR(S): Karathanasis, Sotirios K.; Oettgen, Peter; Haddad, Issam A.; Antonarakis, Stylianos E.

CORPORATE SOURCE: Dep. Cardiol., Child. Hosp., Boston, MA, 02115, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1986), 83(22), 8457-61  
CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The genes coding for 3 proteins of the plasma lipid transport system, apolipoproteins A1 (APOA1), C3 (APOC3), and A4 (APOA4), are closely linked and tandemly organized on the long arm of human chromosome 11. The human APOA4 gene was isolated and characterized. In contrast to APOA1 and APOC3 genes, which contain 3 introns, the APOA4 gene contains only 2. An intron interrupting the 5' noncoding region of the APOA1 and APOC3 mRNAs is absent from the corresponding position of the APOA4 mRNA. However, similar to APOA1 and APOC3 genes, the introns of the APOA4 gene sep. nucleotide sequences coding for the signal peptide and the amphipathic domains in APOA4. These results suggest that the APOA1, APOC3, and APOA4 genes were derived from a common evolutionary ancestor and indicate that during evolution the APOA4 gene lost one of its ancestral introns. Two restriction endonuclease sites, an XbaI located in the 2nd intron of the APOA4 gene and a different XbaI located 9 kilobases 3' to the APOA4 gene, are polymorphic in Mediterranean and Northern European populations. Haplotype anal. indicated that even though these polymorphic sites are located within 9 kilobases they do not display significant nonrandom assocn. Finally, restriction mapping anal. of DNA from a patient with combined APOA1-APOC3 deficiency and premature coronary artery disease indicated that this patient has a structurally normal APOA4 gene.

IT 102305-80-6 102305-81-7

RL: PRP (Properties)

(amino acid sequence of)

L17 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1986:419642 HCAPLUS

DOCUMENT NUMBER: 105:19642

TITLE: Structure, evolution, and tissue-specific synthesis of human apolipoprotein AIV

AUTHOR(S): Karathanasis, Sotirios K.; Yunis, Ivan; Zannis, Vassilis I.

CORPORATE SOURCE: Harvard Med. Sch., Child. Hosp., Boston, MA, 02115, USA

SOURCE: Biochemistry (1986), 25(13), 3962-70

CODEN: BICHAW; ISSN: 0006-2960

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Apolipoprotein AIV (apoAIV) is a protein of the lipid transport system found assocd. with chylomicrons, high-d. lipoprotein (HDL), and the lipoprotein-free fraction of the plasma. The gene coding for the human apoAIV is closely linked with the genes coding for apolipoprotein AI (apoAI) and CIII (apoCIII). A nearly full-length apoAIV cDNA clone was isolated by screening an adult human liver library with a human apoAIV gene probe. In-frame translation of the cDNA sequence in this clone indicated that the human apoAIV consists of 396 amino acid residues, including a 20-residue-long signal peptide. In addn., the coding region of this cDNA sequence contains 15 66-base-pair (bp) repeats, 11 of which code for amino acid repeats with potentials of forming amphipathic helices. Alignment and comparison of the human and rat apoAIV amino acid sequences indicated a 5-residue deletion near the C-terminus of the rat protein. This comparison also indicated that these proteins are 61.8% homologous, suggesting that the rate of evolution of apoAIV is 65 accepted point mutations (PAMs)/100 residues/100 million years. The rates of evolution of certain amino acid repeats in apoAIV are higher than the rate of evolution of the entire protein. However, the corresponding, computer-generated, secondary structures and hydropathy profiles of these repeats are very similar between the human and rat apoAIV. The relative steady-state levels of apoAIV mRNA in various human and monkey tissues were detd. by hybridization blotting anal. of total RNA, from these tissues, with a human apoAIV cDNA probe. This anal. showed that only fetal and adult intestine and pancreas as well as adult but not fetal liver contain detectable amts. of apoAIV mRNA. These results indicate that the apoAIV gene evolved by amplification of an ancestral 66-bp sequence coding for a peptide with amphipathic properties and that conservation of the secondary structure and hydropathic properties of certain domains in apoAIV may be significant for the function(s) of this protein. Furthermore, these results indicate that in humans and nonhuman primates, apoAIV mRNA synthesis occurs primarily in intestine and, to a lesser extent, in pancreas, whereas in liver apoAIV mRNA synthesis may be regulated by developmental and(or) nutritional factors.

IT 102305-80-6 102305-81-7

RL: PRP (Properties)

(amino acid sequence of)

L17 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1986:162776 HCAPLUS

DOCUMENT NUMBER: 104:162776

TITLE: The nucleotide and derived amino acid sequence of human apolipoprotein A-IV mRNA and the close linkage of its gene to the genes of apolipoproteins A-I and C-III

AUTHOR(S): Elshourbagy, Nabil A.; Walker, David W.; Boguski, Mark S.; Gordon, Jeffrey I.; Taylor, John M.

CORPORATE SOURCE: Dep. Physiol., Univ. California, San Francisco, CA, 94140-0608, USA

SOURCE: Journal of Biological Chemistry (1986), 261(5), 1998-2002

CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Both cDNA and genomic clones encoding human apolipoprotein (apo-) A-IV were isolated and characterized. Southern blot analyses of apo-A-IV gene-contg. cosmids revealed that the apo-A-IV gene is linked to the apo-A-I and apo-C-III genes within a 20-kilobase span of chromosome 11 DNA. The apo-A-IV gene is located .apprx.14 kilobases downstream from the apo-A-I gene in the same orientation, with the apo-C-III gene located between them in the opposite orientation. The nucleotide sequence of the



corresponding human apo-A-IV mRNA was detd., and the derived amino acid sequence showed that mature plasma apo-A-IV contained 376 residues. Throughout most of its length, human apo-A-IV contained multiple tandem 22-residue repeated segments with amphipathic, .alpha.-helical potential. Amino acid substitutions within these homologous segments were generally conservative in nature. A comparison of the sequence of human and rat apo-A-IV revealed a 79% identity of amino acid positions in the N-terminal 60 residues and a 58% identity in the remainder of the sequences, with the human protein contg. 5 extra residues near the C terminus. The distribution of apo-A-IV mRNA in different tissues of the rat, marmoset, and man showed that apo-A-IV mRNA was abundant in both the liver and small intestine of the rat, but abundant only in the small intestine of the marmoset and man. Only trace amts. of the mRNA were found in all other tissues that were examd. The structure and expression of apo-A-IV and the close linkage of its gene to those for apo-A-I and apo-C-III suggest a regulatory relationship among the 3 genes.

IT

101551-39-7

RL: PRP (Properties)

(amino acid sequence of)